Proline residues in the transmembrane /extracellular domain interface loops have different behaviours in 5-HT_3 and nACh receptors

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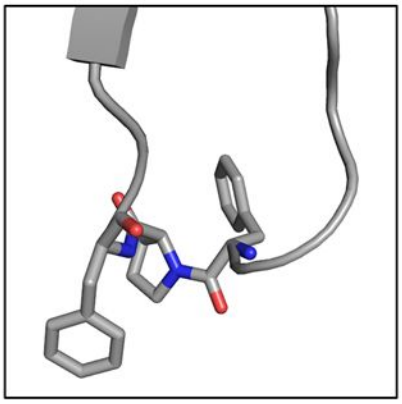
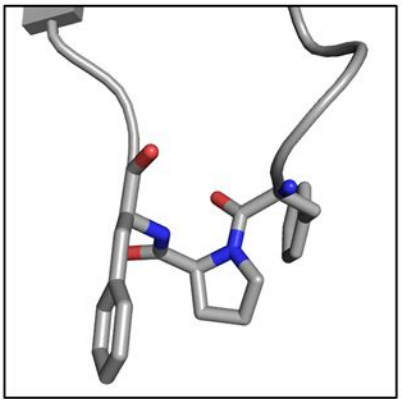
Supporting Information

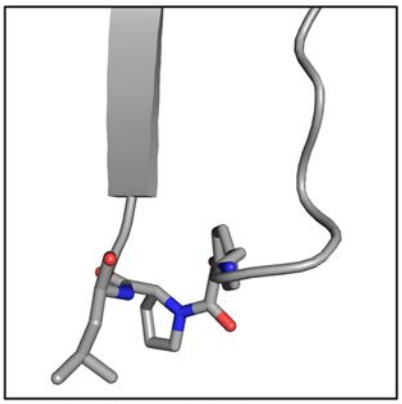
List of materials: Figures S1-S4



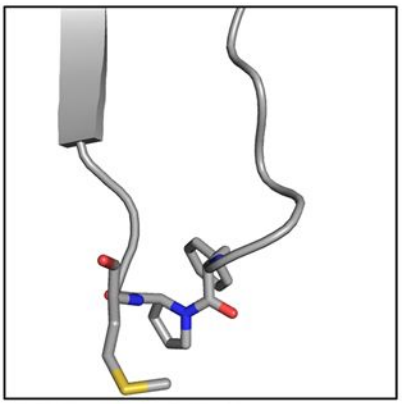
PDB ID: 5KXI
Receptor: α4ß2 nAChR
Pro conformation: *cis*



PDB ID: 6HIQ
Receptor: 5-HT_3AR
Pro conformation: trans

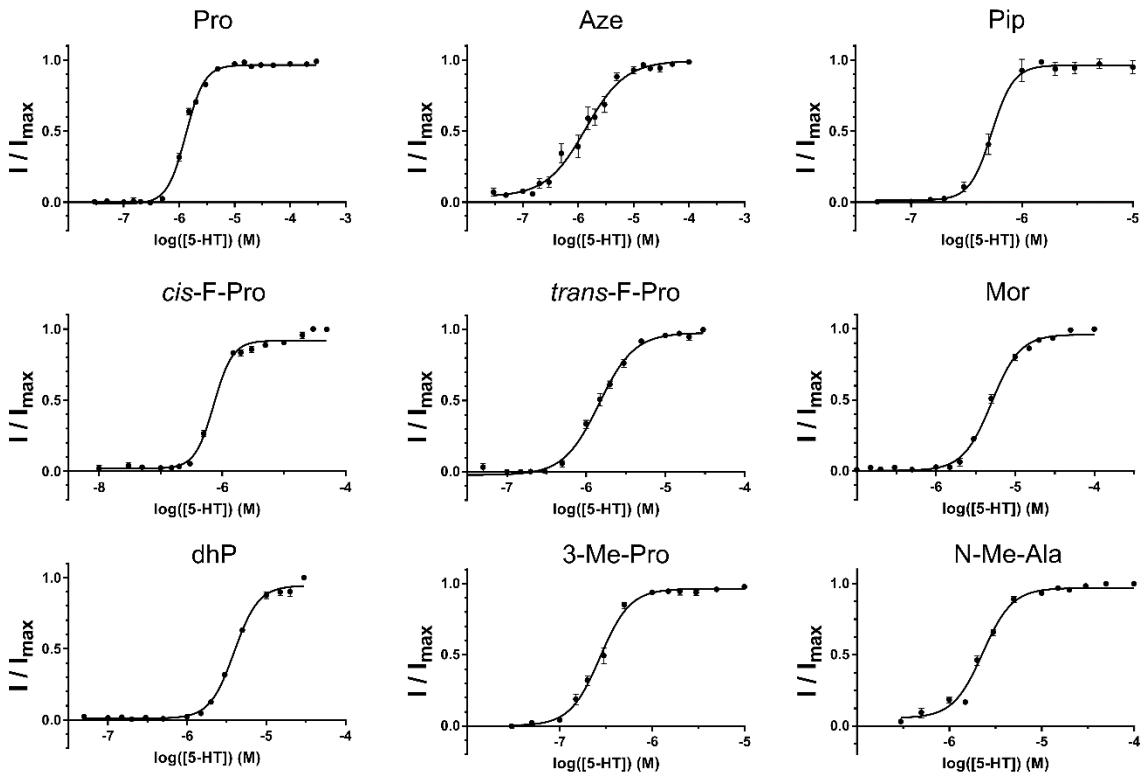


PDB ID: 4COF
Receptor: $GABA_A$R ß3
Pro conformation: *cis*

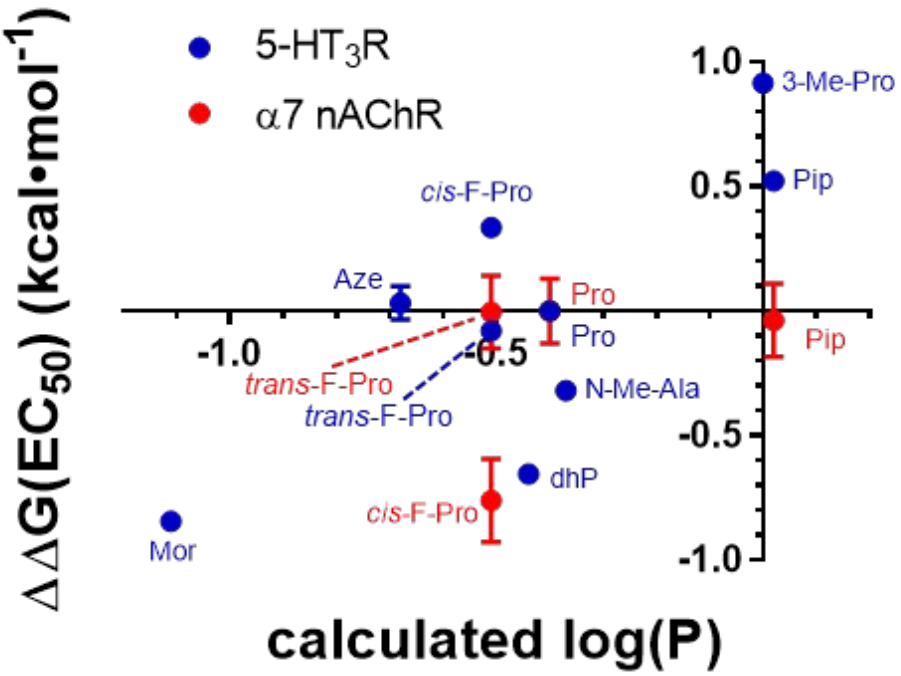


PDB ID: 5VDH
Receptor: α3 GlyR
Pro conformation: *cis*

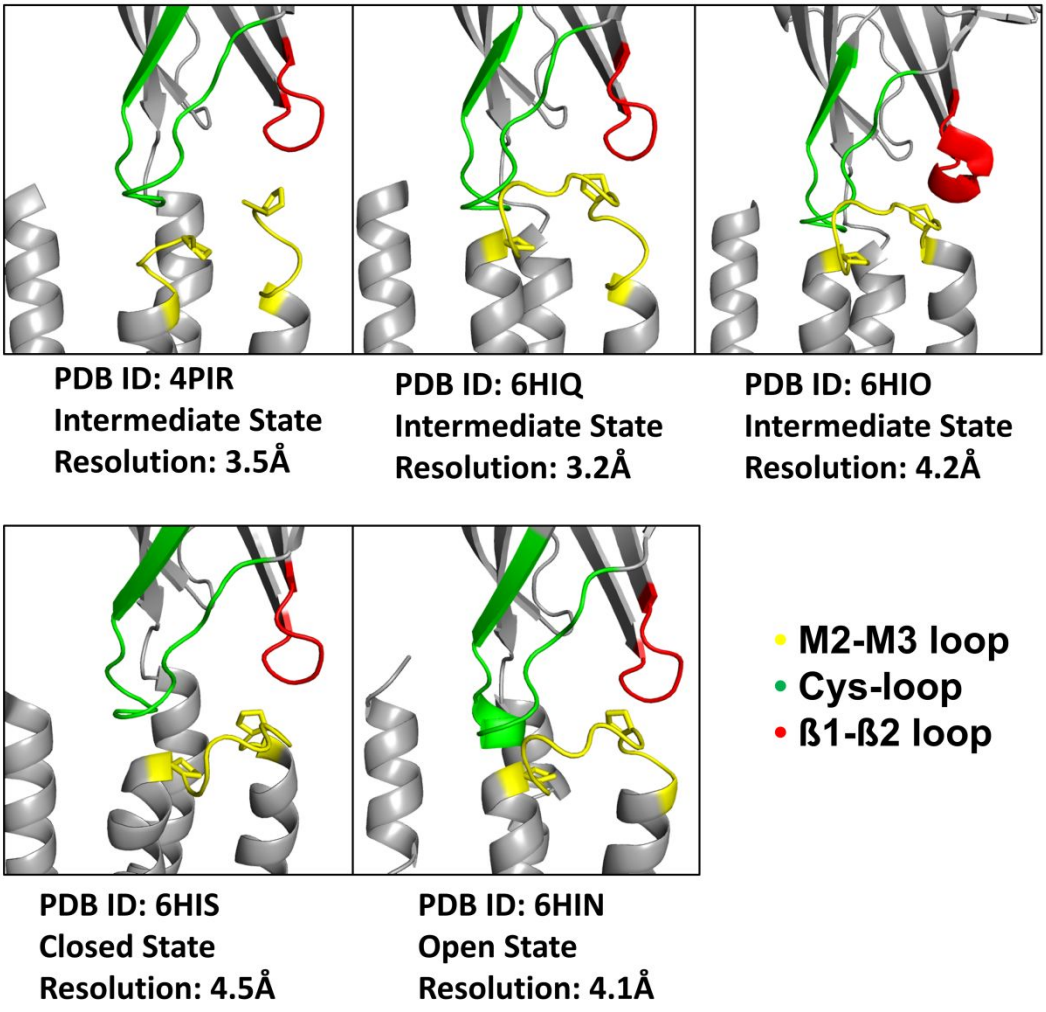
Supplementary Figure S1. A selection of Cys-loop receptor X-ray and cryo-EM structures demonstrating that both *cis* and *trans* peptide bonds are viable at the conserved Cys-loop proline in different receptors.



Supplementary Figure S2. Concentration-response plots for 5-HT_3R with non-canonical amino acids successfully incorporated at the Cys-loop Pro. Data are mean ± SEM, n=4-23.



Supplementary Figure S3. Plot showing there is no correlation between logP and receptor function in 5-HT_3R and nAChR incorporating various amino acid substitutions at the Cys-loop Pro. Data are shown as mean ± SEM, n=4-23, however the marker size often exceeds the size of the error bars.



Supplementary Figure S4. Structures of the 5-HT_3R showing the ß1-ß2 loop close to the M2-M3 loop.